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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,256	ZHAO ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The art unit location of your application and examiner has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652, Examiner Richard Hutson Ph.D.

Applicants cancellation of claims 17-22 in Paper No. 4, 2/8/2002, is acknowledged. Claims 1-16 are pending and present for examination.

It is noted that in applicants previous amendment, Paper No. 4, 2/8/2002, on page 2, under "Version with Markings to show Changes Made", applicants state that "claims 1-16 are cancelled.' This statement is disregarded in light of applicants earlier statement in the same paper in which applicants state "Please cancel claims 17-22. Claims 1-16 are pending." Thus, claims 1-16 are pending and present for examination.

Priority

Applicants statement on the first line of the specification that "Pursuant to 35 U.S.C. 119 (e), this application is a continuation of U.S. Patent Application No. 09/411,351, filed October 1, 1999, the disclosure of which is herein incorporated by reference", is acknowledged, however, applicants claim of under 35 U.S.C. 119 (e) is questioned as it is believed that the referred to statute should be either 35 U.S.C. 120 of 121, not 119(e) which is reserved for claims of priority to provisional applications. Further application 09/411,351 has issued as U.S. Patent No. 6,300,073 and it is suggested that applicants amend the application to reflect these changes.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

It is noted that no information disclosure statements have bee filed with the current application.

Specification

The disclosure is objected to because of the following informalities:

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into this application by reference to PCT/US99/13305 at page 7, second paragraph, is improper because said document discloses a preferred embodiment, *i.e.*, "[a] preferred thermostable enzyme".

The use of the trademarks TWEEN 20, TRITON X-100, NONIDET P40 (NP40) have been noted in this application. They should be capitalized wherever they appear and be accompanied by their generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.
The disclosure is objected to because of the following informalities: The specification needs to reflect the current status of applications that have been sited therein.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s): Page 7, line 8 of the specification lists the amino acid sequence "MRGHEX_1GLX_2" for which there is no sequence identifier or sequence listing.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-4 and 9-11 are indefinite in that it is unclear when a "mutant DNA polymerase" is a mutant Taq polymerase (claims 2-4 and 9-11) or when a "mutant DNA polymerase" ceases to be a mutant Taq polymerase and thus is a different type of mutant DNA polymerase. Because of this "indefiniteness" the scope of the genus claimed is unclear.

Claims 5-7 are similarly indefinite as discussed above for claims 2-4 and 9-11, with respect to "mutant Taq polymerase ", in that it is unclear when a "mutant reverse transcriptases" is a mutant moloney leukemia virus reverse transcriptase or when a "mutant reverse transcriptases" ceases to be a mutant mutant moloney leukemia virus reverse transcriptase and thus is a different type of mutant reverse transcriptase. Because of this "indefiniteness" the scope of the genus claimed is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-16 are directed to all possible enzyme compositions comprising a mutant thermostable DNA polymerase and a mutant reverse transcriptase (claims 1, 12-16), wherein said mutant DNA polymerase is a N-terminal deletion mutant Taq polymerase (claims 2-4), and wherein said mutant reverse transcriptase is a point mutant of moloney murine leukemia virus reverse transcriptase (claims 5-7), and those enzyme compositions further comprising an antibody specific for said mutant thermostable DNA polymerase (claims 8-11). There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these enzymes compositions by any identifying structural characteristics or properties other than the activities recited in claims 1, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 8-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claims 8-12 is drawn to an enzyme composition comprising (i) an N-terminal deletion mutant of *Taq* polymerase, (ii) a point mutation mutant of a moloney murine leukemia reverse transcriptase; and (iii) an antibody specific for said N-terminal deletion mutant of *Taq* polymerase.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The amount of experimentation needed to practice the claimed invention is significant- on the order of several man years with little if any reasonable expectation of success.

The Amount of Direction or Guidance Provided

The specification does not provide any guidance where the claimed enzyme composition is to be used in a reproducible manner.

The Presence or Absence of Working Examples

The specification provides but one example and that does not address the use of the claimed enzyme composition.

The Nature of the Invention

The invention relates to the art of chemistry and physiology. These are areas recognized by the court as being highly unpredictable and deserving of greater levels of disclosure. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art is fairly well developed in so far as one is conducting a RT-PCR reaction. However, the use of an antibody in such a reaction speaks to an unpredictable element that has not been developed in the art. Specifically, the reaction conditions for performing an amplification reaction requires the imposition of denaturing conditions (so to dissociate complementary strands of nucleic acid). Such conditions would in effect denature the antibody, rendering it useless. The specification is silent as to how this antibody-containing mixture is to be effectively and reproducibly used in such a reaction.

The Relative Skill of Those in the Art

The relative skill of those in the art most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

Breadth of the Claims

The claims have sufficient breadth of scope so to encompass any mixture of a terminal deletion mutant of *Taq* polymerase, a point mutation of a moloney murine leukemia virus reverse transcriptase, any antibody, or mixtures of same, which are specific for said N-terminal deletion mutant of *Taq* polymerase, as well as any additional reagent. For the reasons set forth above, the specification has not been found to set forth in sufficient detail the manner by which the claims enzyme composition is to be used and as such has failed to enable same. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

" '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').

"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

"It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

For the above reasons, and in the absence of convincing evidence to the contrary, the specification has not been found to enable said claims and as such stand rejected under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> *A person shall be entitled to a patent unless –*
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Mizutani et al. (Microbiol. Immunol., Vol 42 (8), pp 549-553, 1998)

Mizutani et al., disclose an enzyme composition comprising a reverse transcriptase and a *Taq* polymerase. Said enzyme composition is described as enabling 'single-step RT-PCR." As a result of their having combined these two well-known enzymes, they have provided "a most practical method for reducing the risk of contamination during manipulations, saving both time and labor." Further, the enzyme composition gives rise to "a practical and highly sensitive single-step RT-PCR method." The enzymes recited in said publication are considered to meet the limitations of the enzymes recited in the claims.

The aspect of preparing the reagents and practicing the disclosed method of RT-PCR speaks to the reagents, including buffers, dNTPs, etc., in a common vessel. Such speaks to the presence of a "kit."

If per chance the publication does not teach one or more of the claimed limitations explicitly, said publication is considered to make such obvious as the use of one modified enzyme for another which has the same properties is considered to be functional equivalents thereof and satisfy the requirements of obviousness.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,300,073 B1. An obvious type double patenting rejection is appropriate where conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g.., *In re* Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re* Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re* Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-21 of U.S. Patent No. 6,300,073 B1, drawn to a enzyme composition and kit comprising: as mutant thermostable DNA polymerase comprising the amino acid sequence $MRGHEX_1GLX_2$ proximal to the N-terminus and a mutant reverse transcriptase, anticipates claims 1-16 of the instant application.

Remarks

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
9/30/2003